PATENT
Attorney Docket No. 06267.0132-00000

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| In re Application of: | ) | |
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| Antti HAAPALINNA et al. | ) | Group Art Unit: 1614 |
| | ) | |
| Application No.: 10/552,892 | ) | Examiner: Savitha M. RAO |
| | ) | |
| § 371 Date: November 26, 2007 | ) | |
| | ) | Confirmation No.: 4440 |
| For: TREATMENT OF EPILEPSY | ) | |
| | ) | |

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

**RESPONSE TO RESTRICTION REQUIREMENT**

In a restriction requirement dated January 5, 2009, the Examiner required the election of a species under PCT Rule 13.1. Restriction Requirement at 2. Applicants provisionally elect with traverse atipamezole. At least claims 1, 2, and 7 read on that elected species.

Applicants respectfully assert that there is unity of invention under the PCT Rule 13.1 standard. To be sure, the International Searching Authority concluded that there was not unity of invention because the uniting technical feature, the alpha2-adrenoceptor antagonist property, "has been already described in the state of the art." Written Opinion of the International Searching Authority at Sheet 2 ( "Written Opinion, "a copy of is enclosed for the Examiner's convenience.) Although the international examiner used the appropriate standard, Applicants respectfully assert that the present rejection should not be maintained because the rejection was impermissibly based on "a

narrow, literal, or academic approach," and did not give "the benefit of any doubt [] to the applicant." *See* M.P.E.P. § 1850. While it is unnecessary to argue the patentability of the present claims over art that the Examiner has not yet raised, Applicants provide initial arguments why the international examiner incorrectly concluded that the prior art cited undermined the unity of invention.

In particular, four documents were cited in the Written Opinion to support the international examiner's rejection all of which are of record in the present application:

- Pitkanen, A. et al. "Disease Modifying Effects of Alpha2-adrenoceptor Blocker, Atimpamezole on Epileptogenesis in Rats," *Epilepsia* (2003) 44(Supp. 8):75 ("Pitkanen" referred to by the Int'l examiner as XP8031700);
- Mirski, M. A. Z., et al. "Dexmedetomidine Decreases Seizure Threshold in a Rat Model of Experimental Generalized Epilepsy," *Anesthesiology* (1994) 81:1422-1428 ("Mirski" referred to by the Int'l examiner as XP8031693);
- EP 0 194 984; and
- EP 0 304 910.

As an initial matter, Applicants respectfully point out that Pitkanen is not prior art to the present application. Pitkanen was published on December 1, 2003, and is based on a conference that occurred on October 12-16, 2003. The present application claims priority to U.S. Provisional Patent Application No. 60/461,413, filed on April 10, 2003. Therefore, neither any disclosure at the conference nor the printed abstract is prior art

to the present application, and its teachings are irrelevant to the question of unity of invention.

Furthermore, the remaining documents, as a whole, do not teach that alpha2-adrenoceptor antagonists treat epilepsy. The international examiner contends that Mirski "discloses that atipamezole is able to reverse the proconvulsant action of dexmedetomidine [an alpha2 agonist]." Written Opinion at Sheet 2. Mirski does state that atipamezole "block[ed] the proconvulsant behavioral action at both doses of DEX . . ." Mirski at Abstract. However, the international examiner ignored the rest of the document where it is taught that "atipamezole alone ***did not*** alter background EEG, nor did it affect the clonic convulsant threshold." *Id.* (emphasis added). Moreover, the authors noted that atipamezole exhibited similar results to the control, *id.* at 1425; *see also* Fig. 1, and "[a]ntagonism at the $\alpha_2$-receptor, for example, has been associated with a ***proconvulsant*** effect." *Id.* at 1426 (emphasis added). Therefore, there is no teaching in Mirski that atipamezole treats or would treat epilepsy. Indeed, as shown in Figure 1, atipamezole exhibited an effect almost identical to that of the control mice where no drug besides PTZ was added.

EP 0 194 984 teaches that "[c]ertain compounds according to the invention also possess interesting pharmacological activities concerning the central nervous system, for example, anticonvulsive activity, ***whether or not associated with an effect on α-adrenergic receptors***." EP 0 194 984 at page 8, lines 14-18. Therefore, EP 0 194 984 does not teach that alpha2-adrenoceptors are effective for treating epilepsy. Indeed, the alpha2-adrenoceptor antagonist effect shown in Table 1 does not directly correlate with the anticonvulsive effect shown in that same table. At best, EP 0 194 984 teaches

that some of the compounds falling within the scope of its disclosure, whether or not alpha2 antagonists or agonist (because both are taught), have an anticonvulsant effect.

EP 0 304 910 does disclose that compounds according to its disclosure may be used to treat epilepsy, but epilepsy is in a list of various central nervous system disorders that may be treated. And, there is no data showing the anticonvulsant effect of any of the compounds disclosed in EP 0 304 910. Moreover, EP 0 304 910 was published before Mirski, which disclosed that it had been shown that alpha2 antagonism was proconvulsant. Therefore, taken as a whole, the prior art does not teach that alpha2-adrenoceptor antagonists can be used to treat epilepsy.

Consequently, the uniting feature of the present claims is not undermined, and Applicants respectfully request that the Examiner withdraw the species election and examine the entire claim scope. Under PCT unity practice, an Examiner "should not raise objection of lack of unity of invention merely because the inventions claimed are classified in separate classification groups or merely for the purpose of restricting the international search to certain classification groups." M.P.E.P. § 1850. Therefore, the Examiner's contention that searching in different classes may be required is not enough to support a unity of invention rejection under PCT Rule 13.1 when, as has been shown, here that the prior art does not teach the unifying technical feature. Therefore, for this additional reason, the election requirement should be withdrawn.

Please grant any extensions of time required to enter this response and charge any additional required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: February 3, 2009

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